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=> s adzyme
L1            2 ADZYME

=> s fusion (w) protein and catalytic (w) domain and target and targeting (w) domain
L2           11 FUSION (W) PROTEIN AND CATALYTIC (W) DOMAIN AND TARGET AND TARGE
               TING (W) DOMAIN

=> s chimeric (w) protein and catalytic (w) domain and target and targeting (w)
domain
L3            0 CHIMERIC (W) PROTEIN AND CATALYTIC (W) DOMAIN AND TARGET AND
               TARGETING (W) DOMAIN

=> d ibib abs l2 1-11

L2   ANSWER 1 OF 11     MEDLINE on STN
ACCESSION NUMBER:    95318049     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 7541032
TITLE:               T cell-targeted immunofusion proteins from Escherichia
                     coli.
AUTHOR:              Better M; Bernhard S L; Williams R E; Leigh S D; Bauer R J;
                     Kung A H; Carroll S F; Fishwild D M
CORPORATE SOURCE:    XOMA Corporation, Santa Monica, California 90404, USA.
SOURCE:              The Journal of biological chemistry, (1995 Jun 23) Vol.
                     270, No. 25, pp. 14951-7.
                     Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         199507
ENTRY DATE:          Entered STN: 19950817
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NEWS	4	DEC 23	New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/ USPAT2
NEWS	5	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS	6	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS	7	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS	8	JAN 17	IPC 8 in the WPI family of databases including WPIFV
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NEWS	11	FEB 21	STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS	12	FEB 22	Status of current WO (PCT) information on STN
NEWS	13	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS	14	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS	15	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS	16	FEB 28	MEDLINE/LMEDLINE reload improves functionality
NEWS	17	FEB 28	TOXCENTER reloaded with enhancements
NEWS	18	FEB 28	REGISTRY/ZREGISTRY enhanced with more experimental spectral property data
NEWS	19	MAR 01	INSPEC reloaded and enhanced
NEWS	20	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes
NEWS	21	MAR 08	X.25 communication option no longer available after June 2006
NEWS	22	MAR 22	EMBASE is now updated on a daily basis

NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
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Last Updated on STN: 19960129
Entered Medline: 19950731

AB **Fusion proteins** between cell-**targeting** **domains** and cytotoxic proteins should be particularly effective therapeutic reagents. We constructed a family of immunofusion proteins linking humanized Fab, F(ab')2, or single chain antibody forms of the H65 antibody (which recognizes the CD5 antigen on the surface of human T cells) with the plant ribosome-inactivating protein gelonin. We reasoned that such an immunofusion would kill human **target** cells as efficiently as the previously described chemical conjugates of H65 and gelonin (Better M., Bernhard, S. L., Fishwild, D. M., Nolan, P. A., Bauer, R. J., Kung, A. H. C., and Carroll, S. F. (1994) J. Biol. Chemical 269, 9644-9650) if both the recognition and **catalytic** **domains** remained active, and a proper linkage between domains could be found. Immunofusion proteins were produced in Escherichia coli as secreted proteins and were recovered directly from the bacterial culture supernatant in an active form. All of the immunofusion proteins were purified by a common process and were tested for cytotoxicity toward antigen-positive human cells. A 20-60-fold range of cytotoxic activity was seen among the fusion family members, and several **fusion** **proteins** were identified which are approximately as active as effective chemical conjugates. Based on these constructs, immunofusion avidity and potency can be controlled by appropriate selection of antibody domains and ribosome-inactivating protein.

L2 ANSWER 2 OF 11 MEDLINE on STN
ACCESSION NUMBER: 94224796 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8170960
TITLE: Functionally active **targeting domain** of the beta-adrenergic receptor kinase: an inhibitor of G beta gamma-mediated stimulation of type II adenylyl cyclase.
AUTHOR: Inglese J; Luttrell L M; Iniguez-Lluhi J A; Touhara K; Koch W J; Lefkowitz R J
CORPORATE SOURCE: Department of Medicine, Howard Hughes Medical Institute, Duke University Medical Center, Durham, NC 27710.
CONTRACT NUMBER: HL16037 (NHLBI)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1994 Apr 26) Vol. 91, No. 9, pp. 3637-41.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199406
ENTRY DATE: Entered STN: 19940613
Last Updated on STN: 20021218
Entered Medline: 19940601

AB The beta-adrenergic receptor kinase (beta ARK) phosphorylates its membrane-associated receptor substrates, such as the beta-adrenergic receptor, triggering events leading to receptor desensitization. beta ARK activity is markedly stimulated by the isoprenylated beta gamma subunit complex of heterotrimeric guanine nucleotide-binding proteins (G beta gamma), which translocates the kinase to the plasma membrane and thereby **targets** it to its receptor substrate. The amino-terminal two-thirds of beta ARK1 composes the receptor recognition and **catalytic** **domains**, while the carboxyl third contains the G beta gamma binding sequences, the **targeting** **domain**. We prepared this domain as a recombinant His6 **fusion** **protein** from Escherichia coli and found that it had both independent secondary structure and functional activity. We demonstrated the inhibitory properties of this domain against G beta gamma activation of type II adenylyl cyclase both in a reconstituted system utilizing Sf9 insect cell membranes and in a permeabilized 293 human embryonic kidney

cell system. Gi alpha-mediated inhibition of adenylyl cyclase was not affected. These data suggest that this His6 **fusion protein** derived from the carboxyl terminus of beta ARK1 provides a specific probe for defining G beta gamma-mediated processes and for studying the structural features of a G beta gamma-binding domain.

L2 ANSWER 3 OF 11 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1995:362428 BIOSIS
DOCUMENT NUMBER: PREV199598376728
TITLE: T Cell-targeted Immunofusion Proteins from Escherichia coli.
AUTHOR(S): Better, Marc [Reprint author]; Bernhard, Susan L.; Williams, Robert E.; Leigh, Scott D.; Bauer, Robert J.; Kung, Ada H. C.; Carroll, Stephen F.; Fishwild, Dianne M.
CORPORATE SOURCE: Xoma Corp., 1545 17th St., Santa Monica, CA 90404, USA
SOURCE: Journal of Biological Chemistry, (1995) Vol. 270, No. 25, pp. 14951-14957.
CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Aug 1995
Last Updated on STN: 30 Aug 1995

AB **Fusion proteins** between cell-**targeting domains** and cytotoxic proteins should be particularly effective therapeutic reagents. We constructed a family of immunofusion proteins linking humanized Fab, F(ab')-2, or single chain antibody forms of the H65 antibody (which recognizes the CD5 antigen on the surface of human T cells) with the plant ribosome-inactivating protein gelonin. We reasoned that such an immunofusion would kill human **target** cells as efficiently as the previously described chemical conjugates of H65 and gelonin (Better M., Bernhard, S. L., Fishwild, D. M., Nolan, P. A., Bauer, R. J., Kung, A. H. C., and Carroll, S. F. (1994) J. Biol. Chemical 269, 9644-9650) if both the recognition and **catalytic domains** remained active, and a proper linkage between domains could be found. Immunofusion proteins were produced in Escherichia coli as secreted proteins and were recovered directly from the bacterial culture supernatant in an active form. All of the immunofusion proteins were purified by a common process and were tested for cytotoxicity toward antigen-positive human cells. A 20-60-fold range of cytotoxic activity was seen among the fusion family members, and several **fusion proteins** were identified which are approximately as active as effective chemical conjugates. Based on these constructs, immunofusion avidity and potency can be controlled by appropriate selection of antibody domains and ribosome-inactivating protein.

L2 ANSWER 4 OF 11 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1994:304464 BIOSIS
DOCUMENT NUMBER: PREV199497317464
TITLE: Functionally active **targeting domain** of the beta-adrenergic receptor kinase: An inhibitor of G-beta-gamma-mediated stimulation of type II adenylyl cyclase.
AUTHOR(S): Inglese, J. [Reprint author]; Luttrell, L. M. [Reprint author]; Iniguez-Lluhi, J. A.; Touhara, K. [Reprint author]; Koch, W. J. [Reprint author]; Lefkowitz, R. J. [Reprint author]
CORPORATE SOURCE: Dep. Med., Box 3821, Howard Hughes Med. Inst., Duke University Med. Center, Durham, NC 27710, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1994) Vol. 91, No. 9, pp. 3637-3641.
CODEN: PNASA6. ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English

ENTRY DATE: Entered STN: 13 Jul 1994
Last Updated on STN: 24 Aug 1994

AB The beta-adrenergic receptor kinase (beta-ARK) phosphorylates its membrane-associated receptor substrates, such as the beta-adrenergic receptor, triggering events leading to receptor desensitization. beta-ARK activity is markedly stimulated by the isoprenylated beta-gamma subunit complex of heterotrimeric guanine nucleotide-binding proteins (G-beta-gamma), which translocates the kinase to the plasma membrane and thereby **targets** it to its receptor substrate. The amino-terminal two-thirds of beta-ARK1 composes the receptor recognition and **catalytic domains**, while the carboxyl third contains the G-beta-gamma binding sequences, the **targeting domain**. We prepared this domain as a recombinant His-6 **fusion protein** from Escherichia coli and found that it had both independent secondary structure and functional activity. We demonstrated the inhibitory properties of this domain against G-beta-gamma activation of type II adenylyl cyclase both in a reconstituted system utilizing Sf9 insect cell membranes and in a permeabilized 293 human embryonic kidney cell system. G-ialpha-mediated inhibition of adenylyl cyclase was not affected. These data suggest that this His-6 **fusion protein** derived from the carboxyl terminus of beta-ARK1 provides a specific probe for defining G-beta-gamma-mediated processes and for studying the structural features of a G-beta-gamma-binding domain.

L2 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:656920 CAPLUS
DOCUMENT NUMBER: 123:81252
TITLE: T cell-targeted immunofusion proteins from Escherichia coli
AUTHOR(S): Better, Marc; Bernhard, Susan L.; Williams, Robert E.; Leigh, Scott D.; Bauer, Robert J.; Kung, Ada H. C.; Carroll, Stephen F.; Fishwild, Dianne M.
CORPORATE SOURCE: XOMA Corp., Santa Monica, CA, 90404, USA
SOURCE: Journal of Biological Chemistry (1995), 270(25), 14951-7
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Fusion proteins** between cell-**targeting domains** and cytotoxic proteins should be particularly effective therapeutic reagents. We constructed a family of immunofusion proteins linking humanized Fab, F(ab')2, or single chain antibody forms of the H65 antibody (which recognizes the CD5 antigen on the surface of human T cells) with the plant ribosome-inactivating protein gelonin. We reasoned that such an immunofusion would kill human **target** cells as efficiently as the previously described chemical conjugates of H65 and gelonin if both the recognition and **catalytic domains** remained active, and a proper linkage between domains could be found. Immunofusion proteins were produced in Escherichia coli as secreted proteins and were recovered directly from the bacterial culture supernatant in an active form. All of the immunofusion proteins were purified by a common process and were tested for cytotoxicity toward antigen-pos. human cells. A 20-60-fold range of cytotoxic activity was seen among the fusion family members, and several **fusion proteins** were identified which are approx. as active as effective chemical conjugates. Based on these constructs, immunofusion avidity and potency can be controlled by appropriate selection of antibody domains and ribosome-inactivating protein.

L2 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:502907 CAPLUS

DOCUMENT NUMBER: 121:102907
TITLE: Functionally active **targeting domain** of the β-adrenergic receptor kinase: an inhibitor of Gβγ-mediated stimulation of type II adenylyl cyclase
AUTHOR(S): Inglese, J.; Luttrell, L. M.; Iniguez-Lluhi, J. A.; Touhara, K.; Koch, W. J.; Lefkowitz, R. J.
CORPORATE SOURCE: Howard Hughes Med. Inst., Duke Univ., Durham, NC, 27710, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1994), 91(9), 3637-41
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The β-adrenergic receptor kinase (βARK) phosphorylates its membrane-associated receptor substrates, such as the β-adrenergic receptor, triggering events leading to receptor desensitization. The βARK activity is markedly stimulated by the isopropenylated βγ subunit complex of heterotrimeric guanine nucleotide-binding proteins (Gβγ), which translocates the kinase to the plasma membrane and thereby **targets** it to its receptor subunits. The amino-terminal two-thirds of βARK1 composes the receptor recognition and **catalytic domains**, while the carboxyl third contains the Gβγ binding sequences, the **targeting domain**. The authors prepared this domain as a recombinant His6 **fusion protein** from Escherichia coli and found that it had both independent second structure and functional activity. The authors demonstrated the inhibitory properties of this domain against Gβγ activation of type II adenylyl cyclase both in a reconstituted system utilizing Sf9 insect cell membranes and in a permeabilized 293 human embryonic kidney cell system. Giα-mediated inhibition of adenylyl cyclase was not affected. These data suggest that this His6 **fusion protein** derived from the carboxyl terminus of βARK1 provides a specific probe for defining Gβγ-mediated processes and for studying the structural features of a Gβγ-binding domain.

L2 ANSWER 7 OF 11 LIFESCI COPYRIGHT 2006 CSA on STN
ACCESSION NUMBER: 96:19231 LIFESCI
TITLE: T cell-targeted immunofusion proteins from Escherichia coli
AUTHOR: Better, M.; Bernhard, S.L.; Williams, R.E.; Leigh, S.D.; Bauer, R.J.; Kung, A.H.C.; Carroll, S.F.; Fishwild, D.M.
CORPORATE SOURCE: Xoma Corp., 1545 17th St., Santa Monica, CA 90404, USA
SOURCE: J. BIOL. CHEM., (1995) vol. 270, no. 25, pp. 14591-14597. ISSN: 0021-9528.
DOCUMENT TYPE: Journal
FILE SEGMENT: F; W3
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **Fusion proteins** between cell-**targeting domains** and cytotoxic proteins should be particularly effective therapeutic reagents. We constructed a family of immunofusion proteins linking humanized Fab, F(ab') sub(2), or single chain antibody forms of the H65 antibody (which recognizes the CD5 antigen on the surface of human T cells) with the plant ribosome-inactivating protein gelonin. We reasoned that such an immunofusion would kill human **target** cells as efficiently as the previously described chemical conjugates of H65 and gelonin if both the recognition and **catalytic domains** remained active, and a proper linkage between domains could be found. Immunofusion proteins were produced in Escherichia coli as secreted proteins and were recovered directly from the bacterial culture supernatant in an active form. All of the immunofusion proteins were purified by a common process and were tested for cytotoxicity toward antigen-positive human cells. A 20-60-fold range of cytotoxic activity was

seen among the fusion family members, and several **fusion proteins** were identified which are ap proximately as active as effective chemical conjugates. Based on these constructs, immunofusion avidity and potency can be controlled by appropriate selection of antibody domains and ribosome-inactivating protein.

L2 ANSWER 8 OF 11 BIOTECHNO COPYRIGHT 2006 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1995:25189002 BIOTECHNO
TITLE: T cell-targeted immunofusion proteins from Escherichia coli
AUTHOR: Better M.; Bernhard S.L.; Williams R.E.; Leigh S.D.; Bauer R.J.; Kung A.H.C.; Carroll S.F.; Fishwild D.M.
CORPORATE SOURCE: Xoma Corp., 1545 17th St.,Santa Monica, CA 90404, United States.
SOURCE: Journal of Biological Chemistry, (1995), 270/25 (14951-14957)
CODEN: JBCHA3 ISSN: 0021-9258
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1995:25189002 BIOTECHNO
AB **Fusion proteins** between cell-**targeting domains** and cytotoxic proteins should be particularly effective therapeutic reagents. We constructed a family of immunofusion proteins linking humanized Fab, F(ab').sub.2, or single chain antibody forms of the H65 antibody (which recognizes the CD5 antigen on the surface of human T cells) with the plant ribosome-inactivating protein gelonin. We reasoned that such an immunofusion would kill human **target** cells as efficiently as the previously described chemical conjugates of H65 and gelonin (Better M., Bernhard, S. L., Fishwild, D. M., Nolan, P. A., Bauer, R. J., Kung, A. H. C., and Carroll, S. F. (1994) J. Biol. Chemical 269, 9644-9650) if both the recognition and **catalytic domains** remained active, and a proper linkage between domains could be found. Immunofusion proteins were produced in Escherichia coli as secreted proteins and were recovered directly from the bacterial culture supernatant in an active form. All of the immunofusion proteins were purified by a common process and were tested for cytotoxicity toward antigen-positive human cells. A 20-60-fold range of cytotoxic activity was seen among the fusion family members, and several **fusion proteins** were identified which are approximately as active as effective chemical conjugates. Based on these constructs, immunofusion avidity and potency can be controlled by appropriate selection of antibody domains and ribosome- inactivating protein.

L2 ANSWER 9 OF 11 BIOTECHNO COPYRIGHT 2006 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1994:24139486 BIOTECHNO
TITLE: Functionally active **targeting domain** of the β-adrenergic receptor kinase: An inhibitor of G(βγ)-mediated stimulation of type II adenylyl cyclase
AUTHOR: Inglese J.; Luttrell L.M.; Iniguez-Lluhi J.A.; Touhara K.; Koch W.J.; Lefkowitz R.J.
CORPORATE SOURCE: Department of Medicine, Howard Hughes Medical Institute, Duke University Medical Center,Durham, NC 27710, United States.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1994), 91/9 (3637-3641)
CODEN: PNASA6 ISSN: 0027-8424
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1994:24139486 BIOTECHNO

AB The β-adrenergic receptor kinase (βARK) phosphorylates its membrane- associated receptor substrates, such as the β-adrenergic receptor, triggering events leading to receptor desensitization. βARK activity is markedly stimulated by the isoprenylated βγ subunit complex of heterotrimeric guanine nucleotide-binding proteins (G(βγ)), which translocates the kinase to the plasma membrane and thereby **targets** it to its receptor substrate. The amino-terminal two-thirds of βARK1 composes the receptor recognition and **catalytic domains**, while the carboxyl third contains the G(βγ) binding sequences, the **targeting domain**. We prepared this domain as a recombinant His.sub.6 **fusion protein** from Escherichia coli and found that it had both independent secondary structure and functional activity. We demonstrated the inhibitory properties of this domain against G(βγ) activation of type II adenylyl cyclase both in a reconstituted system utilizing Sf9 insect cell membranes and in a permeabilized 293 human embryonic kidney cell system. G(iα)-mediated inhibition of adenylyl cyclase was not affected. These data suggest that this His.sub.6 **fusion protein** derived from the carboxyl terminus of βARK1 provides a specific probe for defining G(βγ)-mediated processes and for studying the structural features of a G(βγ)-binding domain.

L2 ANSWER 10 OF 11 EMBASE

ACCESSION NUMBER: 95190741 EMBASE
DOCUMENT NUMBER: 1995190741
TITLE: T cell-targeted immunofusion proteins from Escherichia coli.
AUTHOR: Better M.; Bernhard S.L.; Williams R.E.; Leigh S.D.; Bauer R.J.; Kung A.H.C.; Carroll S.F.; Fishwild D.M.
CORPORATE SOURCE: Xoma Corp., 1545 17th St.,Santa Monica, CA 90404, United States
SOURCE: Journal of Biological Chemistry, (1995) Vol. 270, No. 25, pp. 14951-14957. .
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 950718
Last Updated on STN: 950718

AB **Fusion proteins** between cell-**targeting domains** and cytotoxic proteins should be particularly effective therapeutic reagents. We constructed a family of immunofusion proteins linking humanized Fab, F(ab')2, or single chain antibody forms of the H65 antibody (which recognizes the CD5 antigen on the surface of human T cells) with the plant ribosome-inactivating protein gelonin. We reasoned that such an immunofusion would kill human **target** cells as efficiently as the previously described chemical conjugates of H65 and gelonin (Better M., Bernhard, S. L., Fishwild, D. M., Nolan, P. A., Bauer, R. J., Kung, A. H. C., and Carroll, S. F. (1994) J. Biol. Chemical 269, 9644-9650) if both the recognition and **catalytic domains** remained active, and a proper linkage between domains could be found. Immunofusion proteins were produced in Escherichia coli as secreted proteins and were recovered directly from the bacterial culture supernatant in an active form. All of the immunofusion proteins were purified by a common process and were tested for cytotoxicity toward antigen-positive human cells. A 20-60-fold range of cytotoxic activity was seen among the fusion family members, and several **fusion**

proteins were identified which are approximately as active as effective chemical conjugates. Based on these constructs, immunofusion avidity and potency can be controlled by appropriate selection of antibody domains and ribosome- inactivating protein.

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ACCESSION NUMBER: 94142823 EMBASE
DOCUMENT NUMBER: 1994142823
TITLE: Functionally active **targeting domain** of the β-adrenergic receptor kinase: An inhibitor of G(βγ)-mediated stimulation of type II adenylyl cyclase.
AUTHOR: Inglese J.; Luttrell L.M.; Iniguez-Lluhi J.A.; Touhara K.; Koch W.J.; Lefkowitz R.J.
CORPORATE SOURCE: Department of Medicine, Howard Hughes Medical Institute, Duke University Medical Center,Durham, NC 27710, United States
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1994) Vol. 91, No. 9, pp. 3637-3641. .
ISSN: 0027-8424 CODEN: PNASA6
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 940602
Last Updated on STN: 940602

AB The β-adrenergic receptor kinase (βARK) phosphorylates its membrane- associated receptor substrates, such as the β-adrenergic receptor, triggering events leading to receptor desensitization. βARK activity is markedly stimulated by the isoprenylated βγ subunit complex of heterotrimeric guanine nucleotide-binding proteins (G(βγ)), which translocates the kinase to the plasma membrane and thereby **targets** it to its receptor substrate. The amino-terminal two-thirds of βARK1 composes the receptor recognition and **catalytic domains**, while the carboxyl third contains the G(βγ) binding sequences, the **targeting domain**. We prepared this domain as a recombinant His6 **fusion protein** from Escherichia coli and found that it had both independent secondary structure and functional activity. We demonstrated the inhibitory properties of this domain against G(βγ) activation of type II adenylyl cyclase both in a reconstituted system utilizing Sf9 insect cell membranes and in a permeabilized 293 human embryonic kidney cell system. G(iα)-mediated inhibition of adenylyl cyclase was not affected. These data suggest that this His6 **fusion protein** derived from the carboxyl terminus of βARK1 provides a specific probe for defining G(βγ)-mediated processes and for studying the structural features of a G(βγ)-binding domain.

=> s l2 and trypsin
L4 0 L2 AND TRYPSIN